REMARKS/ARGUMENTS

By this Amendment, claims 1, 3-4, 6-7, 10, 13 are amended. Claims 1-16 are pending.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2005/0154052 (Parthasaradhi et al.). Support for the amendment to claims 3-4, and 6-7 can be found throughout the Specification as filed, and specifically in ¶[0010]. Support for the amendment to claims 10 and 13 can be found throughout the Specification as filed, and specifically in ¶[0010].

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Rejection under 35 USC 102(b)

Claims 1-4, 6-7, and 15 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by US 4,943,590 (Boegesoe et al.). This rejection is respectfully traversed.

In Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (MPEP 2131), the CAFC set forth that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference". In the instant case, not every element of the claims is present in the '590 Boegesoe patent.

Here, the Examiner admits that the instant claims and the prior art disclosure different in the measurements of crystallinity by powdered X-ray diffraction, but argues that the innate nature of a product, such as the X-ray diffraction pattern does not demarcate from a product which although was not measured by X-ray but are allegedly made by the same identical process of crystallization from acetone as allegedly claimed. However, the claims are directed to a novel

polymorphic form of (S)-citalopram, which are not crystallized from acetone, but are instead crystallized from ethyl acetate, methyl tert-butyl ether or acetonitrile. If the Examiner is arguing that the '590 Boegesoe patent inherently discloses the crystalline form of (S)-citalopram oxalate as instantly claimed, then the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Here, the Examiner has not met that burden by arguing that Applicant needs to show the absence of an alleged effect. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

In addition, there is no basis for this assumption. The Examiner cites several references, and argues that it is well recognized in the art that X-ray diffraction patter although useful must be carefully evaluated (See US Pharmacopia), that small difference in X-ray lines does not necessarily imply new forms. The Examiner further alleges that it is well known that powder X-ray pattern are unreliable without factual evidence in comparative measurements that artifacts are

not at issue (see Davidovich et al.) and the same crystal when taken in powdered process can provide misleading pattern (see Bernstein p. 118) while same X-ray pattern can be different compounds.

However, the references cited by the Examiner teach that XRPD is reliable. The Bernstein reference teaches (Bernstein at page 117):

> In the case of polymorphic mixtures, or the determination of polymorphic purity, the choice of analytical method is considerably more restricted, and X-ray diffraction is one of the most definitive techniques.

Additionally, the Davidovich reference teaches (Davidovich at page 12):

> Powder X-ray diffraction is one of the most useful and widely used analytical methods to determine polymorphs and quantify the forms present in a mixture. Detection limit determination becomes critical in the analysis of mixtures. The sensitivity to detect small amounts of a given phase relative to another is critical in the characterization of polymorphs especially for patent infringement cases.

Furthermore the US Pharmacopia teaches (US Pharmacopia at page 1843):

> The powder methods provide an advantage over other means of analysis in that they are usually nondestructive in nature (specimen preparation is usually limited to grinding to ensure a randomly oriented sample, and deleterious effects of X-rays on solid pharmaceutical compounds are not commonly encountered). The principal use of single crystal diffraction data is for the determination of molecular weights and analysis of crystal structures at the atomic level. However, diffraction established for a single crystal can be used to support specific powder pattern as being, truly representative of a single phase.

In addition, the use of different solvents will produce different crystalline forms of a product. For example, U.S. Patent Application Publication No. 2004/0102523 (Broquaire et al.) is directed to a process for obtaining crystalline forms of the enantiomers of modafinil, and the

crystalline forms which it is possible to obtain according to this process. The '523 publication discloses that "[i]n this method, the nature of the solvent selected and the conditions of crystallization selected can be used to direct the preparation of any of the polymorphic forms. Crystallization solvents and conditions will be disclosed hereinafter for each modafinil form, respectively I, III, IV and VII obtained according to this method" ¶[0109]. Therefore, the assumption that crystallization from ethyl acetate, methyl tert-butyl ether or acetonitrile will yield the same polymorphic form as crystallization from acetone has no basis in fact. In addition, claim 15 is directed to a pharmaceutical composition comprising a stable crystalline form, and thus the claimed pharmaceutical composition is not disclosed in the '590 Boegesoe patent.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-4, 6-7, and 15 under 35 USC 102(b) is respectfully requested.

Rejection under 35 USC 102(e)

Claims 10, 13, 16 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by US 6,916,941 (Christensen et al.). This rejection is respectfully traversed.

The Examiner admits that the instant claims and the prior art disclosure different in the measurements of crystallinity by powdered X-ray diffraction, but argues that the innate nature of a product, such as the X-ray diffraction pattern does not demarcate from a product which although was not measured by X-ray but are allegedly made by the same identical process of crystallization from acetone. The Examiner cites several references, and argues that it is well recognized in the art that X-ray diffraction patter although useful must be carefully evaluated.

However, as set forth above, the references cited by the Examiner demonstrate that XRPD is a reliable technique to determine polymorphs.

In addition, while the '941 Christensen patent discloses a method for the manufacture of crystalline particles of escitalopram oxalate by crystallization from ethanol, in the method of synthesis of Form II (S)-citalopram oxalate of the instant claims is not dissolved from ethanol or acetone, but from methanol or isopropyl alcohol. As set forth above, the use of different solvents will produce different crystalline forms of a product.

Therefore, the assumption that crystallization from methanol or isopropyl alcohol will yield the same polymorphic form as crystallization from acetone or ethanol has no basis in fact. In addition, claim 16 is directed to a pharmaceutical composition comprising a stable crystalline form, and thus the claimed pharmaceutical composition is not disclosed in the '941 Christensen patent.

Accordingly, reconsideration and withdrawal of the rejection of claims 10, 13, and 16 under 35 USC 102(e) is respectfully requested.

Rejection under 35 USC 103(a)

Claims 1-16 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over US 4,943,590 (Boegesoe et al.) or US 6,916,941 (Christensen et al.), in view of Cheronis supplemented with US 6,960,613 (Sanches et al.), US 6,768,011 (Rock et al.) or US 7,112,686 (Humble et al.). This rejection is respectfully traversed.

The Examiner argues that the difference between the instant claims and the prior art product is that the powdered X-ray diffraction pattern was included or a variation of solvent was

employed in preparing the product, and that Cheronis taught that crystallization/recrystallization is a routine laboratory tool in purifying compounds. The Examiner further argues that the employment of variation of common laboratory solvent would be a routine operation for such process (see p. 31-33), and that Sanches '613 taught that for the particular compound citalopram oxalate, the same obvious routine recrystallization skill in purification is desirable (see col. 3, lines 30-35), that Rock et al. '011 disclosed the employment of acetone for crystallization (see col. 6, line 1), and that Humble et al. (102(e) reference) taught that recrystallization of enantiomeric citalopram oxalate can employ alcohols, ketones, acetonitrile etc. (see col. 5, lines 22-25, col. 6, lines 8-11).

However, the claims are patentable over the combination of '590 Boegesoe and '941 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble references for the following reasons. To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991). MPEP 2143. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in

judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (KSR v Teleflex, 12 S.Ct. 1727, 1740 (US 2007)). Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. (*Id.*).

Here, not every element of the claims is taught or suggested in the combination of the '590 Boegesoe and '941 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble references. The instant claims are directed to a novel polymorph of (S)-citalopram oxalate. However, the prior art relied upon by the examiner does not teach or suggest the specific polymorphs as claimed by Applicant. The examiner failed to demonstrate that the prior art even recognized that the claimed compound exists in different polymorphic forms, or that there is a known or obvious way to manufacture the specific polymorphic form claimed. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic (see above). Here, the Examiner has assumed, without providing any evidence that the methods of producing (S)-citalopram oxalate in the '590 Boegesoe patent can be altered to produce the claimed polymorphs. However, there is no basis for this assumption because, as set forth above, the use

of different solvents will produce different crystalline forms of a product (see U.S. Patent Application Publication No. 2004/0102523 (Broquaire et al.). Therefore, the assumption that crystallization from ethyl acetate, methyl tert-butyl ether, acetonitrile, methanol or isopropyl alcohol will yield the same polymorphic form as crystallization from acetone or ethanol has no basis in fact.

In addition, there is no motivation for one of skill in the art to alter the methods of the '590 Boegesoe patent to arrive at the claimed method, and no reasonable expectation of success. There is no teaching or suggestion within the '941 Christensen in view of Cheronis supplemented with '613 Sanches, '011 Rock or '686 Humble references to alter the method as taught by the '590 Boegesoe patent to arrive at the instantly claimed method. The Examiner argues that one having ordinary skill in the art is well aware of all the pertinent art in the field. The above references provided the particular process to obtain the crystalline forms of (S)-citalopram oxalate with suggestions that further purification is desirable using routine recrystallization skill with common laboratory solvents. Further motivated by the operable solvents employed by analogous art, the particular choices among the common laboratory solvents are well delineated and suggested. However, the '590 Boegesoe patent does not disclose or suggest methods of preparation of (S)-citalopram oxalate crystalline forms wherein the solvent is ethyl acetate, methyl tert-butyl ether, acetonitrile, methanol or isopropyl alcohol. Since the reference does not disclose or suggest this, there is no motivation to employ the process taught by the'590 Boegesoe patent to crystallize (S)-citalopram oxalate and expect to obtain the desired product to reach the limitations of the claims, with the claimed polymorphic form, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-16 under 35 USC 103(a) is respectfully requested.

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For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
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Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.